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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,403	09/12/2003	Andrew Vaillant	16051-4US	6672

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EXAMINER	
HURT, SHARON L	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,403	VAILLANT ET AL.	
	Examiner	Art Unit	
	Sharon Hurt	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/14/2007 and 6/22/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/14/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the Pre-Appeal Brief Request for Review filed on May 15, 2007, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Response to Amendment

The amendment after final rejection filed on June 22, 2007 has been entered. New claims 44 and 45 have been added subsequent to the final rejection.

Status of the Claims

Claims 1-43 have been cancelled. New claims 44 and 45 are pending and under examination.

Affidavits/Declaration

The declaration under 37 CFR 1.132 filed June 22, 2007 is insufficient to overcome the new grounds of rejection of new claims 44 and 45 previously claims 28 and 29 based upon enablement as set forth below.

Terminal Disclaimer

The terminal disclaimer filed on May 14, 2007 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154 to 156 and 173 of U.S. copending Application No. 10/661,403 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Arguments

The rejection of claims 28 and 29 under 35 U.S.C. 102(b) as being anticipated by Andreola et al. is withdrawn. Applicant's arguments, filed June 22, 2007, with respect to claims 28-29 have been fully considered and are persuasive.

The rejection of claims 28 and 29 under 35 U.S.C. 102(e) as being anticipated by Peyman et al. is withdrawn. Applicant's arguments with respect to claims 28 and 29 have been fully considered and are persuasive.

The rejection of claims 28 and 29 on the ground of provisional nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 14-32 of copending Application No. 10/661,099, claims 1-38 of copending Application No. 10/661,088 and claims 1-2 and 14-32 of copending Application No. 10/661,415 **are withdrawn**. Applicants Terminal Disclaimer filed May 14, 2007 has overcome the rejection.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification, while being enabling for treatment of viral infections, does not reasonably provide enablement for prophylaxis, which is considered as absolute prevention or elimination of viral infection.

The first paragraph of 35 U.S.C. 112 states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). The factors to be considered in determining whether undue experimentation is

required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those In the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a method for the prophylaxis or treatment of a viral infection in a subject. The claim contains the terms "**prophylaxis**" and "**treatment**". The office interprets "**prophylaxis**" as denoting absolute prevention of infection of even a single cell by a virus and absolute elimination of infection of any cell by a virus.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that oligonucleotide formulations have antiviral activity. The art teaches that oligonucleotides can be used for treating HSV-1, HSV-2, influenza and hepatitis B as described by Peyman et al. However the art does not teach prevention of these viral infections or viruses.

The art teaches that the efficacy of therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective plasma concentrations, solubility in tissues, biotransformation, toxicity, rate of excretion or clearance, and in the case of antivirals, propensity for emergence of resistant strains (see Benet et al., pp. 3-32, in The Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph;

and the paragraph bridging pages 20 and 21. The art further teaches that "the story of drug discovery for viral diseases is replete with failures" (Rice et al., Advances in Pharmacology 33:389-438, 1995; see page 390, first sentence of the third paragraph) and that drugs which are quite effective in the laboratory often reveal disappointing traits in the clinical setting (Rice et al., page 409, last paragraph, second sentence). The art further teaches that while there are antiviral agents which can reduce the incidence of or ameliorate the symptoms of viral infection, there are no treatment methods which can completely prevent viral infection in all cells in every subject and no antiviral agents which can completely eliminate infection in every cell of every subject.

The amount of direction or guidance present and the presence or absence of working examples: The disclosure is limited to a discussion of oligonucleotide formulation, which have antiviral activity. These oligonucleotide formulations are used for treating viral infections wherein the specification has working examples of *in vitro* studies in cell culture. The Declaration of Jean-Marc Juteau presents data for *in vitro* and some *in vivo* experiments as summarized in the table below.

There are no working examples drawn to absolute prevention of viral infection *in vivo* by employing the claimed method and no working examples showing absolute prevention of infection with viruses *in vivo*. Therefore, there is insufficient evidence to ascertain that the claimed compositions actually completely prevent or totally eliminate viral infection in humans.

The breadth of the claims and the quantity of experimentation needed: Because the art teaches a high degree of unpredictability in the ability of antivirals to completely prevent or eliminate viral infection, because the claims encompass absolute prevention and elimination of

all virus infections, and because the specification fails to provide an enabling disclosure for absolute prevention or complete elimination, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention commensurate in scope with the claims.

Summary of the Data Presented in the Declaration of Jean-Marc Juteau:

Family	Virus	REP 2031	REP 2055	VITRO	VIVO	Prophylaxis	Treatment
Flavivirus	HCV	Yes	Yes	Yes	Yes	No	Yes
Hepadna	HBV	Yes	No	Yes	No	No	Yes
	HBV	No	Yes	Yes	Yes	No	Yes
Orthomyxo	Influ A	Yes	No	Yes	Yes	No	Yes
Paramyxo	RSV	Yes	No	Yes	No	No	Yes
Herpes	HSV-1	Yes	Yes	Yes	No	No	Yes
	HSV-2	Yes	No	No	Yes	No	Yes
	CMV	No	No	No	No	No	No
Filoviridae	Ebola	Yes	No	No	Yes	No	Yes

Claims 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification/declaration, while being enabling for treatment of HCV, HBV, Influenza A, RSV, HSV-1, HSV-2 and Ebola does not enable the treatment for infection cause by herpesviridae, hepadnaviridae, filoviridae, flaviridae, orthomyxoviridae and paramyxoviridae. In addition, the data presented in the Declaration of Jean-Marc Juteau may enable for the treatment of HCV, HBV, Influenza A, RSV, HSV-1, HSV-2 and Ebola using REP 2031 does not enable the treatment for Influenza A, RSV, HSV-2, or Ebola using REP 2055. Furthermore, neither REP 2031 nor REP 2055 is enabled for the treatment of CMV. See the data summary listed in the table above. The specification does not enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those In the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a method for the prophylaxis or treatment of a viral infection in a subject comprising administering an oligonucleotide formulation comprising SEQ ID NO; 22 (REP 2031) and SEQ ID NO: 24 (REP

2055) having antiviral activity against herpesviridae, hepadnaviridae, filoviridae, flaviridae, orthomyxoviridae and paramyxoviridae.

The state of the prior art: The art teaches that oligonucleotide formulations have antiviral activity. The art teaches that oligonucleotides can be used for treating HSV-1, HSV-2, influenza and hepatitis B as described by Peyman et al. However, it does not teach treatment of all viruses in the herpesviridae, hepadnaviridae, filoviridae, flaviridae, orthomyxoviridae and paramyxoviridae virus families.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability in the art regarding the structural and functional differences in the oligonucleotide sequences used for antiviral activity, detailed teachings are required in the disclosure to enable the full scope of the claims. Applicant's disclosure is limited to the treatment of: HCV, HBV, Influenza A, RSV, HSV-1, HSV-2 and Ebola using REP 2031; and the treatment of HCV, HBV and HSV-1 using REP 2055. The only working examples are listed in the table above. No examples are provided for the treatment of neither CMV using either REP 2031 or REP 2055. These teachings are absent.

The claimed invention is drawn to two sequences representing REP 2031 and REP 2055. The experimental data presented lacks data for Influenza A, RSV, HSV-2, and Ebola for REP 2055. The data also lacks *in vitro* data for HSV-2 and Ebola and *in vivo* data for RSV and HSV-1. Therefore, the specification/declaration does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The breadth of the claims and the quantity of experimentation needed: Because the invention encompasses oligonucleotide sequences for antiviral activity and because the specification fails to provide guidance as to how to use the claimed method for treatment of viral families other than the viruses listed above, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention commensurate in scope with the claims.

Double Patenting

Claims 44 and 45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 14-15, 17-18, 21-22, 27-29 and 39-42 of copending Application No. 10/661,097. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to a method for the prophylaxis or treatment of a viral infection in a subject comprising administering an oligonucleotide formulation comprising SEQ ID NO; 22 (REP 2031) and SEQ ID NO: 24 (REP 2055) having antiviral activity against HSV-1, HSV-2 or CMV.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

This action is non-final.

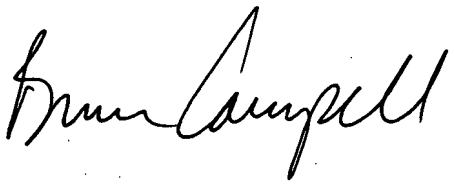
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

September 4, 2007



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